

CRUKAccelerator Award

in Molecular Pathology

(ECMC **ECMC Annual Network Meeting** Thursday 21 May 2015

The King's Fund, No. 11 Cavendish Square, London, WIG 0AN **DRAFT AGENDA**

09:30 - 10:00	Registration and Refreshments						
10:00 - 12:30	Morning Plenary Session - Successful collaborations and patient experience						
10:00 - 10:10	Welcome and introductions						
10:10 - 10:55	ECMCTrial Harmonisation Programme (ETHP) Update: Single Technical Pharmacy Review - by a pharmacist Health Research Authority (HRA) Approval and the Devolved Nations Q&A	Anita Chhabra, Cambridge Janet Messer, HRA					
10:55 - 11:25	Collaborating with industry: the Good, the Bad and the Ugly	Andrew Hughes, Manchester					
11:25 - 11:45	UK Therapeutic Cancer Prevention Network (UKTCPN) Update	Karen Brown, Leicester					
11:45 - 12:05	CRUK Accelerator Award in Molecular Pathology	Manuel Salto-Tellez, Belfast					
12:05 - 12:25	ECMC Patient Experience Survey	ECMC Research Nurse Network Group					
12:25 - 12:30	Concluding Remarks						



Queen's University Belfast

THE NORTHERN IRELAND MOLECULAR PATHOLOGY LABORATORY AND THE NORTHERN IRELAND BIOBANK





2015 will be a good year for Molecular Pathology in the UK

2015 – Molecular Pathology

INITIATIVES

ECMC – CMPath Proposal (Elli & Bridget)

MRC Molecular Pathology Document

RCPath - FRCPath for Clinical Scientists

FUNDING OPPORTUNITIES

MRC Molecular Pathology Nodes

Precision Medicine Catapult

CRUK – Accelerator Award

Print this page



NCRI 2015 Conference Programme

Monday 2 November

08:00-08:45	BACR educational workshop
08:00-08:45	De-mystifying today's science: Dr Elaine Vickers talks you through the main scientific themes of today's programme Elaine Vickers, Science Communicated
08:50-09:00	Introduction to the programme Charles Swanton, Chair of the 2015 Scientific Committee
09:00-09:40	Plenary lecture: Genomics: hype or hope? The future of genomics trials
	Fabrice André, Institut Gustave Roussy, Paris, France
09:40-10:20	Plenary lecture: Big data and patient reported outcome measures (PROMs) <u>Amy Abernethy</u> , Duke University School of Medicine, Durham, USA
10:20-10:50	Networking, exhibition viewing, poster viewing and refreshment break
10:50-12:20	Molecular pathology workshop
	Manuel Salto-Tellez, Queen's University Belfast, UK
10:50-12:20	Symposia and workshops
	Big data Nicholas Luscombe, The Francis Crick Institute, London, UK
	Chromatin, epigenetics and cancer Tony Kouzarides. The Gurdon Institute, University of Cambridge, UK
	Immunotherapy
	Adrian Hayday, King's College London, UK
	Molecular testing in concernening, ready for prime time



Centres Network Accelerator Awards

Our research strategy is built on the understanding that *effective partnerships are crucial for delivering the greatest impact*. We want to support a united Cancer Research UK community in which our Centres work as a network, not just as individual locations.

To support this aim, we have launched a new funding scheme, *the Cancer Research UK Centres Network Accelerator Awards*. These awards provide <u>additional infrastructure</u> support that aim to enable Centres to increase collaboration, promote translational research and build capacity in <u>areas of strategic priority</u> for the Centres and Cancer Research UK. The basic remit and eligibility requirements are:

Maximum of £1m per annum for up to five years

Cancer Research UK Centre directors may lead one application

Centres, Major Centres and other non-centre locations may collaborate on any applications



Scientific Need – the genotyping of tissue-based cellular compartments in cancer

Technical Need – the development of digital molecular pathology as an available commodity in cancer research

Strategic Need – the training of future molecular pathologists

BELFAST CR-UK ACCELERATOR PROPOSAL

Research Resource – A national digital molecular pathology platform to genotype the epithelial-immune compartments in solid tumours, complemented by a comprehensive Clinical Fellowship programme in Molecular Pathology.



THE NORTHERN IRELAND MOLECULAR PATHOLOGY LABORATORY AND THE NORTHERN IRELAND BIOBANK





Lead Institution - Belfast

David Waugh (Centre Director)

Manuel Salto-Tellez (Deputy Centre Director and Molecular Pathology Director)

Peter Hamilton (Digital Pathology Lead)

Jackie James (Molecular Pathologist and Training Lead)

Richard Kennedy (Biomarker Discovery Lead)

Mark Lawler (Associate Director of Postgraduate Studies)

Co-leading Institution - Southampton

Peter Johnson (Centre Director)

Gareth Thomas (Lead Molecular Pathology Immune Response)

Christian Ottensmeier (Immunotherapeutics)

Pandurangam Vijayanand (Micro-transcriptomic & epi immune cell analysis)

Network Members

Sebastian Brandner (UCL Neuropathology)

Andy Hall (Newcastle)

David Gonzalez de Castro (London)

John Le Quesne (Leicester)

Caroline Dive (Manchester)







Test with a Predominant Diagnostic Value			
Sarcoma Translocation Detection			
Lymphoma Translocation Detection			
Clonality Testing			
Test with a Predominant Genetic Value			
Microsatellite Instability Testing			
Mismatch Repair Protein Expression			
Tests with a Predominant Therapeutic Value			
KRAS/NRAS Mutation Testing			
BRAF Mutation Testing			
EGFR Mutation Testing			
ALK Protein Expression			
EML4-ALK Translocation Detection			
Multiple Central Nervous System Molecular Testing			
ER, PR and Her2 Protein Expression			
Her2 Amplification			
<i>c-KIT</i> Mutation Analysis			
PDGFRA Mutation Analysis			

Integrating molecular diagnostics into histopathology training: the Belfast model

C Flynn, ¹ J James, ^{1,2} P Maxwell, ^{1,2} S McQuaid, ^{1,2} A Ervine, ¹ M Catherwood, ³ M B Loughrey, ¹ D McGibben, ¹ J Somerville, ¹ D T McManus, ¹ M Gray, ¹ B Herron, ¹ M Salto-Tellez^{1,2}





Table 1 - Pathology-centred activities in the research endeavour.

Molecular diagnostics in the context of clinical trials Analysis of tissues ahead of molecular analyses Tissue biobanking Digital pathology Pathology informatics Data manager Biomarker validation Integration of validated biomarkers into routine diagnostics

Table 2 - Digital pathology.

Automated digitalization of images for storage and multi-site discussion

Automated scoring of IHC

Automated counting of hybridization signals

Automated identification of tumour in sections for subsequent microdissection

Table 3 - Pathology bioinformatics.

Digital imaging

Pathology integration of pathological data, clinical data and biomarker analytical results

Translation of high-throughput analysis to biomarkers with meaningful diagnostic/clinical relevance

Translation of high-throughput analysis to pathology reports

Review

Molecular pathology - The value of an integrative approach

Manuel Salto-Tellez^{a,b,*}, Jacqueline A. James^{a,b}, Peter W. Hamilton^a

^oNorthern Ireland Molecular Pathology Laboratory, Centre for Cancer Research and Cell Biology, Queen's University, Belfast, Northern Ireland, UK

^bTissue Pathology, Belfast Health and Social Care Trust, Belfast, Northern Ireland, UK





MOLECULAR ONCOLOGY 8 (2014) 1163-1168



Review

Molecular pathology - The value of an integrative approach



Manuel Salto-Tellez^{a,b,*}, Jacqueline A. James^{a,b}, Peter W. Hamilton^a

"Northern Ireland Molecular Pathology Laboratory, Centre for Cancer Research and Cell Biology, Queen's University, Belfast, Northern Ireland, UK ^bTissue Pathology, Belfast Health and Social Care Trust, Belfast, Northern Ireland, UK



UKNEQAS



End to End Diagnostic and Research Service Cutting Across Technologies and Infrastructures



Salto-Tellez et al. Molecular Oncology, 2014







Drug Development

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Biomarker Development

Fig. 9. The role of digital pathology in drug development and companion biomarker discovery and validation.

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Digital pathology and image analysis in tissue biomarker research

Peter W. Hamilton *, Peter Bankhead, Yinhai Wang, Ryan Hutchinson, Declan Kieran, Darragh McArt, Jacqueline James, Manuel Salto-Tellez

Biologing and Informatics, Centre for Canare Research & Cell Biology, Queen's University Bellast, 97 Lisburn Road, Bellast 819 78L, Northern Inland, United Hingdom



HOW TO ADDRESS HETEROGENEITY:

TOPOGRAPHIC HETEROGENEITY: Analyzing as many different parts of the tumor as possible

HISTOGENETIC HETEROGENEITY: Analyzing many cell types as available

TEMPORAL HETEROGENEITY: Analyzing as many samples from the same tumor in the course of time

COMPARTMENTAL HETEROGENEITY: Analyzing as many body compartments as possible, such as primary tumor, circulating tumor cells, and exosomes or plasma.



Salto-Tellez M. In: *Tan & Lynch's Principles of Molecular Diagnostics and Personalized Cancer Therapy,* Lippincott Williams & Wilkins, 2012



Southampton



Therapeutic Targeting of Integrin $\alpha v \beta 6$ in Breast Cancer

Kate M. Moore, Gareth J. Thomas, Stephen W. Duffy, Jane Warwick, Rhian Gabe, Patrick Chou, Ian O. Ellis, Andrew R. Green, Syed Haider, Kellie Brouilette, Antonio Saha, Sabari Vallath, Rebecca Bowen, Claude Chelala, Diana Eccles, William J. Tapper, Alastair M. Thompson, Phillip Quinlan, Lee Jordan, Cheryl Gillett, Adam Brentnall, Shelia Violette, Paul H. Weinreb, Jane Kendrew, Simon T. Barry, Ian R. Hart, J. Louise Jones*, John F. Marshall*



Tumour-infiltrating lymphocytes predict for outcome in HPV-positive oropharyngeal

cancer

M J Ward^{1,2}, S M Thirdborough¹, T Mellows¹, C Riley¹, S Harris³, K Suchak⁴, A Webb⁵, C Hampton⁶, N N Patel², C J Randall², H J Cok⁷, S Jogai⁸, J Primrose⁹, K Piper⁴, C H Ottensmeier^{1,10}, E V King^{1,7,10,11} and G J Thomas^{*,1,8,10,11}



Pandurangam Vijayanand (Micro-transcriptomic & epi immune cell analysis)



Identification and Validation of an Anthracycline/ Cyclophosphamide-Based Chemotherapy Response Assay in Breast Cancer

Jude M. Mulligan, Laura A. Hill, Steve Deharo, Gareth Irwin, David Boyle, Katherine E. Keating, Olaide Y. Raji, Fionnuala A. McDyer, Eamonn O'Brien, Max Bylesjo, Jennifer E. Quinn, Noralane M. Lindor, Paul B. Mullan, Colin R. James, Steven M. Walker, Peter Kerr, Jacqueline James, Timothy S. Davison, Vitali Proutski, Manuel Salto-Tellez, Patrick G. Johnston, Fergus J. Couch, D. Paul Harkin, Richard D. Kennedy



Table 4.Association of the DNA damage response deficiency(DDRD) assay with estrogen receptor (ER) status, HER2 status, andlymphocytic infiltration within validation datasets

		DDRD-	
Adjuvant dataset	Total No.	positive, %	P *
Adjuvant			
ER-positive	112	25.0	<.001
ER-negative	77	52.0	
HER2-positive	46	41.3	.26
HER2-negative	128	32.0	
Triple negative	44	54.6	.001
Non-triple negative	135	28.2	
Lymphocytic infiltrate positive	35	74.3	<.001
Lymphocytic infiltrate negative	155	27.7	
Neoadjuvant			
ER-positive	70	24.3	<.001
ER-negative	134	67.9	

J Natl Cancer Inst. 2014 Jan;106(1):djt335. doi: 10.1093/jnci/djt335.





Pamela J. Maxwell^a, Jonathan Coulter^a, Steven M. Walker^{a,b}, Melanie McKechnie^a, Jessica Neisen^a, Nuala McCabe^b, Richard D. Kennedy^{a,b}, Manuel Salto-Tellez^a, Chris Albanese^c, David J.J. Waugh^{a,*}

20	40	60	80	100	120	Logrank Test P-	Value: 0.005825
		Mor	nths Disease	Free			
				#	total cases	#cases relapsed	median months disease free
Cases with	Alteration	(s) in Query	Gene(s)		87	12	1.41
Cases witho	ut Alteratio	on(s) in Quer	y Gene(s)		66	24	110.16







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Immune Modulation in Cancer with Antibodies

David B. Page,¹ Michael A. Postow,¹ Margaret K. Callahan,¹ James P. Allison,² and Jedd D. Wolchok¹

¹Ladwig Center for Cancer Immunoherapy, Memorial Sloan-Kettering Cancer Center, New York, New York 10005, email: paged@mket.org, postown@mket.org, caliham@mketcomg welchoki@mket.org
²Department of Immunology, M.D. Anderson Cancer Center, Houston, Teass 77040; email: jalihoo@mketchencomg.



Figure 1

Targets of antibody immune modulators. (*a*) Targetable members of the CD28/CTLA-4 immunoglobulin superfamily include cytotoxic T lymphocyte antigen 4 (CTLA-4) (1), programmed cell death protein 1 (PD-1) (5, 7), B and T cell attenuator (BTLA) (84), lymphocyte activation gene 3 (LAG3) (85), and inducible T cell costimulator (ICOS) (86). (*b*) Targetable members of the tumor necrosis factor (TNF) superfamily include CD40 (87, 88), OX40 (89), CD137/4-1BB (90), glucocorticoid-induced TNFR-related protein (GITR) (91), and CD27. (*c*) Programmed cell death 1 ligand 1 (PD-L1). Mel: melanoma. (*d*) Killer inhibitory receptor (KIR). (*e*) T cell Ig and mucin-containing domain 3 (TIM3).



Target 2 DIGITAL PATHOLOGY & GENOMICS



Hamilton P (Salto-Tellez M). Oncotarget 2015 (accepted)









UCL INSTITUTE OF NEUROLOGY

Tumor and Stem Cell Biology

Comparative Expression Analysis Reveals Lineage Relationships between Human and Murine Gliomas and a Dominance of Glial Signatures during Tumor Propagation In Vitro



Nico V. Henriquez¹, Tim Forshew², Ruth Tatevossian², Matthew Ellis¹, Angela Richard-Loendt¹, Hazel Rogers⁵, Thomas S. Jacques³, Pablo Garcia Reitboeck¹, Kerra Pearce⁴, Denise Sheer², Richard G. Grundy⁵, and Sebastian Brandner¹





THE CLINICAL FELLOWSHIP PROGRAMME MSc in Molecular Pathology



BELFAST

CENTRE

MSC HSC Molecular Pathology Curriculum Development Academic Modules

FRCPath Curriculum for Clinical Scientists (in part fulfilment for Modernising Scientific Careers Programme Higher Specialist Scientific Training)

Specialty: MOLECULAR PATHOLOGY

Chair:	Dr George Vassiliou
Contributors:	Professor Manuel Salto-Tellez
	Professor Ian Cree
	Dr John Paul
	Dr Tim Wreghitt
	Dr Martin Barnardo
	Dr Elizabeth Hodges
	Professor Finbarr Cotter
	Dr Mike Scott
	Dr Carolyn Grove
	Dr Rachel Butler
	Dr Fiona MacDonald

Integrating molecular diagnostics into histopathology training: the Belfast model

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Outline of topic	Description	Principles
DNA RNA Proteins NA extraction methods	Overview, structure, replication Transcription, types/structures, RNA polymerases, regulation of transcription, microRNAases Amino acids, genes and genetic code, translation Isolation of DNA and RNA, assessment of quality and quantity of nucleic acids	(nowledge and skills in core molecular technologies and rechniques
PCR	History of PCR, advanced PCR and PCR optimisation, PCR detection and evaluation techniques, limitations of PCR and troubleshooting	Expertise in the molecular pathology of colorectal cancer
Analysis and characterisation of NA Nucleic acid amplification Gene mutations DNA sequencing Molecular oncology High-throughput technologies Validation and optimisation procedures Quality control and quality assurance Regulation in the use of human tissues for research Core skills in slide annotation	Hybridisation technologies, detection systems, results interpretation Target, probe and signal amplification Types, detection and nomenclature of gene mutations Direct sequencing, bioinformatics Analytic targets of molecular testing, gene rearrangements DNA/RNA microarrays, NGS and TGS, whole genome sequencing R&D within molecular diagnostics present and future Discussion of QA and QC in molecular diagnostics Introduction to biobanking, research ethics and research governance within academia and the healthcare setting Be able to identify and annotate areas for macrodissection relevant to downstream testing. Be able to assign percentage tumour content Turkht how to perform tirgue precedurer	Expertise in the molecular pathology of lung cancer Expertise in the molecular pathology of malignant melanoma Expertise in the molecular pathology of gastrointestinal stromal fumours (GISTs) Expertise in the molecular pathology of sarcomas Expertise in the molecular pathology of paediatric cancers, hyroid cancer, central nervous system neoplasias and others Research, development and innovation in molecular pathology eadership and management of a molecular diagnostic
Core skills in DNA extraction	Taught how to perform DNA extraction procedures	aboratory
QA, quality assurance; QC, quality control; NA, nucleic a	scid; NGS, Next Generation Sequencing; TGS, Third Generation Sequencing.	Training and education



JCP Online First, published on February 3, 2014 - Published by group.bmj.com JCP Online First, published on February 3, 2014 as 10.1136/jclinpath-2014-202176

Viewpoint

Integrating molecular diagnostics into histopathology training: the Belfast model

C Flynn,¹ J James,^{1,2} P Maxwell,^{1,2} S McQuaid,^{1,2} A Ervine,¹ M Catherwood,³ M B Loughrey,¹ D McGibben,¹ J Somerville,¹ D T McManus,¹ M Gray,¹ B Herron,¹ M Salto-Tellez^{1,2}





THE CLINICAL FELLOWSHIP PROGRAMME MSc in Molecular Pathology





Speicher MR, Pantel K.Nat Biotechnol. 2014 May;32(5):441-3.



CRUK DIGITAL MOLECULAR PATHOLOGY & TRAINING NETWORK





To create a "common digital pathology language" across the members of the proposal

1.

2.

To use digital pathology to describe tumour heterogeneity and cancer immunology

3.

To improve the efficiency of NGS through digital pathology pre-analytical interventions

4. To develop "digital neuropathology" in CNS oncology

5.

To create a structure of Clinical Fellowships /MSc in different aspects of Molecular Pathology (Including liquid biopsy pathology, lung digital pathology and the pathology of early-phase clinical trials)



True partnership to develop and consolidate molecular pathology in the UK

Focusing on an area of significant need (digital molecular pathology) and with a strong training programme

Attending to a very specific scientific purpose (tissue genotyping of specific cellular compartments)

Partnership (Belfast-Southampton) and a true network

Proposal that has the potential of transforming the molecular pathology scene in the UK

